LETTERS TO THE EDITORS

Regarding "Percutaneous ultrasound guided thrombin injection: A new method for treating postcatheterization femoral pseudoaneurysms"

To the Editors:

A recent article by Kang et al (J Vasc Surg 1998;27:1032-8) reported a new and effective method of treating the problem of false aneurysms after femoral arterial catheterization. Their method, modified and reported by others,[1-3] has several advantages over the standard first-line treatment of ultrasound scan–guided compression repair in that the procedure is quick, involves minimal pain, and has a high success rate, even in patients with large false aneurysms and in patients who are currently undergoing anticoagulation therapy. In the series of patients reported, there were no significant procedure-related complications, in particular, systemic reactions to the thrombin. However, a recent case in our institution has brought this issue to light as more than a theoretical consideration.

A 10-month-old boy was assessed after the development of a pulsatile lump in the antecubital fossa after intravenous cannulation during anesthesia for endoscopy. A duplex scan confirmed a 3 cm–diameter pseudoaneurysm originating from the posterior aspect of the brachial artery with a 3-mm neck and 1.8-cm cavity in continuity with the artery, the remainder of the aneurysm being filled with thrombus. In full, ultrasound scan–guided compression was carried out with general anesthetic for 20 minutes but was unsuccessful. This was followed by a percutaneous injection of thrombin with ultrasound scan guidance. Thrombin (1000 U/mL) was injected slowly with a 25G needle into the center of the cavity to a total of 200 units (0.2 mL). There was immediate thrombosis with highly echogenic clot followed 30 seconds later by an acute and dramatic ischemia of the forearm and hand associated with a loss of the radial pulse and absence of flow in the brachial artery on duplex scan. The mottling improved and the hand became viable in 15 minutes, but the brachial occlusion persisted and it was decided to explore the artery. The thrombus and organized hematoma were successfully removed as shown in Fig 1, and the defect in the artery was repaired with direct suturing. After this, there was restoration of the radial pulse and no subsequent complications.

We believe that this case raises some issues regarding the assessment of patients who may be suitable for this new and appealing option of treatment. The effect may be related to total dosage of thrombin used, the rate of administration, or the size of the neck of the sac, all of which may allow systemic "spillage" of a highly thrombogenic substance. There are no pharmaceutical guidelines on dosages, so small incremental volumes seem reasonable. However, even a small dose entering the arterial circulation may not be neutralized by natural fibrinolysis. It is unknown whether the dose required relates either to the size of the patient or to the size of the pseudoaneurysm being treated. In the event of systemic thrombosis, thrombolysis with tissue plasminogen activator could be administered. This has been successfully used in infants at doses of 0.25 to 0.5 mg/kg/hr after iatrogenic femoral thromboses.[4] However, in an acute severely ischemic limb this may not be justified. The authors describe monitoring for this complication but not their policy of treatment should it occur. It is also difficult to accurately assess with duplex scan whether the neck will allow the passage of thrombin into the native artery, and an alternate technique of inflating an angioplasty balloon at the site of the neck via the contralateral groin to prevent leakage has been described[2] to potentially decrease the risk of this complication. A different method compresses the neck of the sac during the

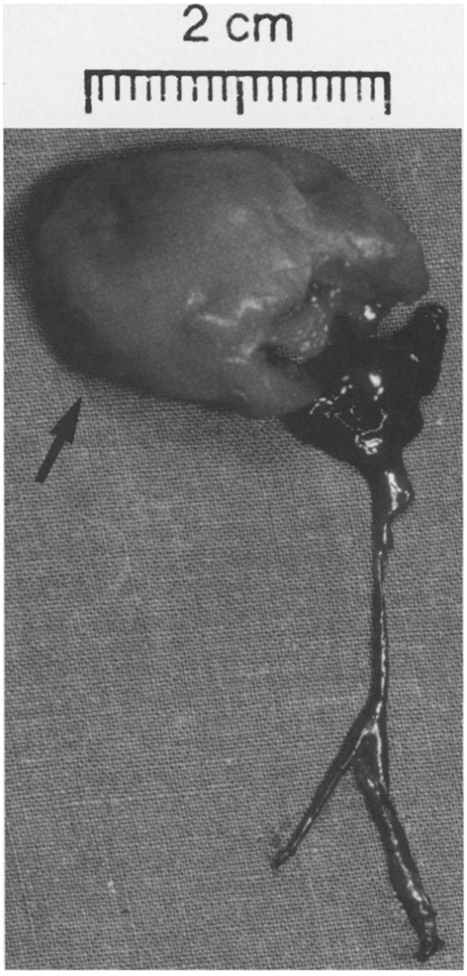

Fig 1. Thrombus removed from brachial artery and pseudoaneurysm cavity with surrounding organized hematoma *(arrow)*.

thrombin injection to prevent leakage.[3] Both these techniques interrupt the flow into the distal artery and into the cavity during injection and may slow the process of thrombosis. All the methods have excellent success rates on small numbers of patients, and therefore, at this stage, no individual technique can be considered superior in terms of efficacy or safety.

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Reply

We would like to thank the editors for the opportunity to respond to the letter by Drs Lennox, Griffen, Nicolaides, and Mansfield. Since the submission of our manuscript describing the initial experience with ultrasound scan–guided thrombin injection, we too have had a complication, but its cause was clear. After 1 injection of 0.5 mL of thrombin into a brachial artery pseudoaneurysm ($1.9 \times 0.8 \times 0.5$ cm), most of the pseudoaneurysm was thrombosed, but there was a persistent neck that was 0.3-cm wide and 0.4-cm long. Having become skilled at needle positioning, we placed the needle tip within this neck and injected another 0.2 mL of thrombin with successful thrombosis. However, a few minutes later, hand ischemia developed in the patient and ultrasound scan showed thrombus occluding the distal brachial artery. The patient was already undergoing anticoagulation therapy with heparin at the time, and an additional 5000 units were given. We scheduled the operating room to perform a thrombectomy, but a few minutes later, the patient's hand ischemia resolved completely. Ultrasound scan showed some residual thrombus along the wall of the brachial artery, and 3 days later, it had completely disappeared. A review of the videotape showed that some of the thrombin solution was injected directly into the artery. On the basis of this experience, we do not further inject persistent necks and 5 necks have been observed, with spontaneous thrombosis in 4 and a recurrent pseudoaneurysm the following day in 1. Overall, we have successfully treated 58 of 59 pseudoaneurysms with this technique.

We have had personal communications with a few other physicians who have encountered thrombosis of the femoral artery with limb ischemia after thrombin injection. All were successfully treated with intra-arterial urokinase infusion. In each case, it seemed that too large a volume (several mL) of thrombin solution was injected. If the volume of thrombin solution injected exceeds the volume of the pseudoaneurysm, it is possible that some of it will be forced into the artery. Too rapid an injection also could cause this problem. We recommend initial injection of a small volume of thrombin, especially for smaller pseudoaneurysms. Currently, we rarely inject more than 0.5 mL. However, we do not think that a more dilute thrombin solution would be necessarily safer. The high concentration that we use causes rapid conversion of the solution into a solid (thrombus) and decreases the possibility that some of the solution will flow into the artery.

The cause of the complication in the case presented by Dr Lennox is less clear. The brachial artery of a 10-month-old child is probably only 2 to 3 mm in diameter. The hole in the artery may have been almost as large as the arterial diameter. After successful thrombosis of the pseudoaneurysm, there would be thrombus filling the neck and covering the arterial defect. Thrombin trapped within thrombus is still active, and therefore, its surface is thrombogenic. Thrombus that forms in response to thrombin injection may be more thrombogenic than naturally occurring thrombus. This thrombogenic material would be exposed to the luminal surface of the artery, and because of the small size of the artery, could comprise a significant portion of the luminal area and cause thrombosis of the artery. For the same reason, the incidence rate of arterial thrombosis after catheterization is higher in infants and in smaller arteries of adults. One could avoid this complication by not using this technique for pseudoaneurysms of small arteries. If the above hypothesis is correct, the maneuvers mentioned by Dr Lennox (compressing the neck or inflating an intra-arterial balloon catheter during thrombin injection) would not prevent this complication. Anticoagulation therapy with heparin during and after thrombin injection may be a better option.

Treatment of this complication needs to be individualized, and the degree of ischemia, the extent and location of the thrombosis, whether the aneurysm is patent or occluded, and the condition of the patient must be taken into consideration. We applaud Dr Lennox and his colleagues for the successful resolution of a difficult complication.

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